Somatosensory findings in postherpetic neuralgia

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Abstract

Somatic sensory perception thresholds (warm, cold, hot pain, touch, pinprick, vibration, two-point discrimination), allodynia and skin temperature were assessed in the affected area of 42 patients with unilateral postherpetic neuralgia (PHN) and 20 patients who had had unilateral shingles not followed by PHN (NoPHN), and in the mirror-image area on the other side. There was no difference between the two groups for age or length of time after the acute herpes zoster infection. The PHN group showed significant changes in all sensory threshold measurements when the affected area was compared with the mirror-image area on the unaffected side, while the NoPHN group exhibited no threshold changes. Mechanical allodynia was present in 87% of the PHN group; half of the 12 patients with ophthalmic PHN showed extension of allodynia to the maxillary distribution. No differences in skin temperature were recorded between affected and unaffected regions in either group. Our findings show a deficit of sensory functions mediated by both large and small primary afferent fibres and also suggest major central involvement in the pathophysiology of the condition. If PHN does not occur following acute herpes zoster, recovery of neural functions appears to be good.

Postherpetic neuralgia (PHN) has been defined as pain in the area of acute shingles persisting or recurring 30 or more days after the acute infection.[1] Several recent reviews concur that its pathogenesis remains largely unknown.[2–5] It is generally accepted that in the acute stages of shingles inflammatory changes occur throughout the sensory nerve from the periphery to the dorsal root. Inflammation is most intense in the dorsal root ganglion where local haemorrhage may occur.[6] Spinal cord changes and anterior root involvement are rarely present.[7]

In contrast, only a few pathological studies exist on postherpetic neuralgia. In 1900, Head and Campbell reported on 21 cases of herpes zoster, 13 of which were examined between 57 and 790 days after the eruption. They described fibrosis of the dorsal root ganglion and secondary sclerosis of the dorsal root and peripheral nerve. They also reported ipsilateral degeneration of the posterior column which "disappeared between five and nine months". However, apart from one vivid description, it is difficult to know whether these cases actually experienced pain or not. Recently, Watson *et al* reported atrophy of the dorsal horn in one case of PHN; atrophic changes extended several segments outside the affected nerve root.[8] To what extent acute changes are reversible in patients recovering from shingles has not been systematically studied. Neither is there any agreement over the actual mechanisms of pain involved. Noordenbos has suggested that pain is associated with a preferential loss of large diameter fibres and relative preservation of small fibres,[9] basing his hypothesis on necropsy studies of four patients. Conversely, Zacks noted eventual degeneration of both small and large fibres.[10] Watson *et al* noticed a reduction of both myelinated and unmyelinated fibres in the dorsal root although they recognise the integrity of at least some unmyelinated fibre input by the lack of change in substance P staining.[8] At present, we acknowledge that although both peripheral and central degenerative changes are present in PHN, the mechanism which leads to relentless pain and not just simple sensory loss, remains obscure.

The clinical picture of postherpetic neuralgia is unique among the non-traumatic neuropathies. Both positive and negative sensory signs can be recognised. There is usually evidence of sensory impairment in one or more dermatomes but there is also inappropriate sensitivity to tactile stimuli, broadly referred to as allodynia, so that lightly stroking the affected skin produces pain whereas firm pressure in the same region does not.[4] Hyperpathia and radiation of pain outside the affected dermatome are well-known features.[5] On the McGill Questionnaire[11] patients described the pain as burning, pricking, lancinating and aching, and itching was also frequently underlined. The word "tender" was usually chosen to describe the allodynia characteristic of the condition (see below).[12] The pain differs from that generated by nociceptor stimulation in being relatively resistant to analgesics including narcotics and other treatments.[13,14] Shingles is one of the commonest neurological diseases, its incidence rate ranging from 1·31 to 3·4 per 1000 person-years.[7,15] Estimates of the risk of PHN lasting a minimum of six months after the rash has disappeared currently range from 2·9% to 21·4%.[16,17] However, elderly patients seem to be especially at risk; 50% of those at age 60 and 75% of those at age 70 develop PHN.[5]

To study the long term sensory impairment in the area involved by zoster infection we employed simple noninvasive quantitative

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somatosensory perception tests suitable for use on an outpatient population.

Material and methods

Patients

Two groups of patients were investigated; patients with PHN and patients who had had shingles in the past but had not developed PHN (NoPHN). All PHN patients attended the Centre for Pain Relief, Walton Hospital, Liverpool, between September 1987 and May 1988. During that time, 42 consecutive patients were admitted to the study. There were no refusals. The diagnosis was arrived at by clinical means (history, typical scars) and agreed upon by at least two specialists. The length of time since the eruption was at least three months.

The NoPHN group of 20 patients was collected from a list supplied by three general practitioners in Liverpool and the local ophthalamological hospital where a recent herpes zoster survey had been carried out.[17] One hundred and five letters were sent to the patients enquiring about the sequelae of the acute shingles. Those who answered were contacted by telephone to ask whether they had pain or not. Twenty four patients volunteered to participate in the study. Four of them were excluded. In two cases there was some doubt as to the actual diagnosis of shingles and no typical scars; in two further cases (thoracic) the diagnosis of shingles seemed tenable but there were no scars at all to guide the examiner. As with PHN patients, the time that had elapsed after the eruption of shingles was at least three months. The final number of patients in this group was 20.

Patients were considered as having PHN if they had spontaneous pain or allodynia, with or without spontaneous pain. Patients with itching only were not considered as PHN subjects. Of the NoPHN group four reported having experienced slight bouts of itching occasionally; they had not consulted their doctor or received any treatment for that and were included in the study. Excluded from both groups were patients with dementia, known peripheral or central nervous system disease, major metabolic diseases, malignancies, alcoholism and subjects who had been subjected to neuroablative procedures for the treatment of PHN.

The aim of the study and the nature of the tests were explained to the patients according to the Helsinki Declaration. An oral or written consent was obtained from all participants.

Table 1 Demographic and clinical data of tested groups

	PHN	*NoPHN*
N	42	20
female:male	21/21	14/6
mean age (SD)	69·6 (9·6)	69·5 (7·5)
mean duration (SD)[1]	32·6 (25·4)	35·5 (27·0)
medication[2]		
none	14	20
AC + AD	12	—
AD + analg	7	—
AC + analg	3	—
analg only	6	—

[1]values in months; [2]AC = anticonvulsant, AD = tricyclic antidepressant, analg = analgesic medication

Table 2 Distribution of zoster in PHN and NoPHN patients

	PHN	*NoPHN*
Ophthalmic	12	10
Cervical	10	0
Upper thoracic	7	4
Lower thoracic	10	5
Lumbar	2	1
Sacral	1	0
Total	42	20

Demographic and clinical data for the two groups are shown in table 1.

Location of zoster in the two groups is shown in table 2. All cases were unilateral, more or less evenly distributed between right and left (as described by Campbell *et al*,[12 18]) and usually affected one or two dermatomes.

Methods

All the tests were carried out at the Pain Relief Foundation, Liverpool. Each patient was clinically examined to rule out any overt neurological disease or dementia. Each patient filled in a pain questionnaire on the history and quality of pain, past treatment, complications, and psychosocial aspects. These data are not considered further in the present report.

Location of PHN or original shingles (in the case of NoPHN) was determined by visible scar tissue which was usually quite prominent in patients with PHN and far less conspicuous in NoPHN subjects. All the measurements were made within the affected zone although in some PHN patients pain was reported beyond the limits of the scar area.

Care was taken to avoid measuring directly over scar tissue. In essence, tests were carried out over the scarless skin within the affected dermatome. Even with the use of a thermode (see below) this proved possible in all tested cases. Wherever possible, the area of maximum pain intensity was determined and measurements were carried out within it. An attempt was also made to define a pain-free area within the affected dermatome(s), but this was only found in three out of 42 cases. It did, however, prove possible to outline an area of minimum pain intensity within each affected dermatome and this was used for the second measurement in each case.

In all cases, the exact counterparts of the test sites on the contralateral (mirror) side were determined and the same tests performed. The testing sequence alternated and in half of the cases the first test carried out was on the mirror side and in half on the affected side. All the patients entered into the study had unilateral zoster only.

Before testing, each patient received a short explanation of the methods used and a short rehearsal was conducted on the dorsal aspect of the forearm. In NoPHN cases only one spot on either side was measured. Testing took approximately 60 minutes to complete.

Warm and cold thresholds were determined

by a commercially available device (Thermotest, Somedic AB, Stockholm, Sweden) which works on the Peltier principle.[19] Briefly, a thermocouple 10 cm^2 in area (for cervical, thoracic and lumbar regions) or 3·6 cm^2 (for facial regions) is warmed up or cooled down at a rate of change of 0·5–1·5 C/s. The testing method is a modification of the Marstock technique.[20] Measurements started from an adapting skin temperature of 30°C after the complete disappearance of any thermal sensation caused by the application of the thermode. The patients responded to each sensation of warm, cold, hot pain or cold pain by pressing a switch which reversed the direction of temperature change and allowed the thermode to return to the initial temperature. A cut off point for the warm threshold was determined at 50·0 C and for the cold threshold at 5°C. Each measurement was carried out 4–6 times in consecutive order and the average value was calculated. In cases where cut off points were reached without the patient recognising any thermal sensation, only one repetition was performed for fear of injuring the skin. A similar procedure was carried out on the contralateral side. In seven patients, a slightly different method was employed. From the adaptation temperature of 30°C the thermode was warmed and cooled alternately; each time the patient perceived either sensation he reversed the current of the thermode (from warm to cold and vice versa). Plateau levels of both thermal thresholds were obtained within a few minutes; they proved to be 2–3°C higher than with the other method.

Hot pain was measured using the same instrumentation. The probe temperature was increased until the patient perceived pain and pressed the switch. This procedure was repeated once and the average of the two calculated. In 22 patients, the thermode was allowed to cool until the patient either perceived pain or the lower limit of the equipment (5°C) was reached. Cold pain was tested only once.

Tactile sensation was measured with von Frey filaments, which were applied in a descending and ascending order of magnitude to assess both the disappearance and appearance thresholds (at least three applications). Care was taken to avoid stroking the skin with the hair and only to do an indentation. The force required to bend each filament (in grams) was converted to log units.

Pinprick sensation was tested with weighted needles. The needles (25 mm 24G needles weighing from 0·2 to 5·2 g) were on plungers of 5 ml plastic syringes moving freely. By holding the syringe the examiner could guide the needle of any weight perpendicularly to the area tested; in practice it was only the weight of the needle that determined the force and consequent pinprick sensation (or lack of it). Similarly to tactile stimulation, this test was carried out in a descending and ascending manner (method of limits) and the threshold determined by the average of three applications.

Two point discrimination was tested conventionally with Weber's compasses, moving the instrument gently over the skin, a method which has been shown to produce more accurate results than simply applying it on the skin.[21] Three ascending and descending series in increments of 5 mm (face) and 10 mm (neck, trunk) were administered in alternating order.

Vibration was tested over a bony part in 14 patients using a hand held fixed-frequency variable-amplitude vibrameter with weight controller (Somedic AB, Stockholm, Sweden). With this method, the threshold is expressed in terms of amplitude of stimulator movement.[22] Both the appearance and disappearance thresholds were determined (in μm) and the average calculated.

Skin temperature was measured using free thermocouples attached to the skin (Digitron Instruments, model 4071, Hertford, United Kingdom). Each patient stayed in the investigation room for at least 20 minutes to acclimatise before the measurement.[23] Liquid crystal contact thermography was also carried out in the affected and nonaffected regions.

The presence of allodynia was assessed by gently applying a battery driven toothbrush (Braun D 3, FRG) on the affected skin area. The brush was found to move back and forth 53 times a minute, with an amplitude of 1·5 mm. We found it easier to hold the handle of the brush without exerting a force in excess of 8 g on the skin surface. The patient reported change in subjective pain sensation, using a visual analogue scale (VAS) for pain[24] with a mobile slider enabling the constant responses to change in intensity to be registered, ranging from 0 to 100 mm. VAS before stimulation and at the height of pain (peak VAS) were recorded, as well as the time taken to reach the peak. The duration of hyperpathia was also recorded. Allodynia was considered to be present if the VAS scale reached 100 mm (whatever the initial level) or if a reading of at least 25 mm above the initial (pretest) level was recorded.

We also studied allodynia in cases of ophthalmic PHN by testing the effect of moving one to three of the stiff hairs in the eyebrow. The response was recorded as painful (allodynic) or non-painful (non-allodynic). Also, using the brush method, maxillary and mandibular divisions on the affected side were tested for the presence of allodynia in these 12 cases.

Hyperalgesia to skin stretch was evaluated in another 12 patients by manually pulling the skin from outside the affected region. Again, the patient's response was recorded as painful or non-painful.

Statistical analysis

The Wilcoxon matched-pairs test was used for a comparison of results between the zoster affected dermatomes and the contralateral dermatomes in both groups. A value of $p < 0·05$ (two-tailed) was considered to be statistically significant.

In addition, we tested 20 healthy subjects (mean age 68·5 (SD) 9·2 years, female:male 12:8) collected from the spouses and relatives of the patients for normative data. In these

Table 3 Threshold medians (and ranges) of the affected and contralateral skin areas in PHN patients (N = 42)

	Affected side	*Unaffected side*
Warm threshold (°C)	40·0 (33·6–50·5)	35·0 (32·1–43·1)
Cold threshold (°C)	25·3 (5·0–34·0)	28·8 (23·3–35·5)
Hot pain threshold (°C)	46·1 (39·6–50·0)	43·2 (36·3–47·7)
Tactile threshold ($\log_{10}$ 0·1 mg)	4·3 (1·7–6·7)	2·8 (1·7–4·9)
Pinprick threshold (g)	5·2 (0·2–5·2)	0·7 (0·2–4·4)
2-point discrimination (cm)	7·0 (1·5–10·0)	3·0 (0·9–9·0)
Vibration threshold (μm)	7·8 (2·8–79·0)	6·8 (2·0–37·0)

All the comparisons are significant ($p < 0·01$, two-tailed; Wilcoxon matched-pairs test)

Table 5 Relative frequency (in percentages) of abnormal sensory perception thresholds in PHN and NoPHN patients

	PHN	*NoPHN*
Warm	68	10
Cold	60	10
Hot pain	60	5
Touch	73	5
Pinprick	78	10
2-point discrimination	62	13
Vibration	27	13

subjects, all the tests (with the exception of cold pain) were carried out bilaterally in the ophthalmic, cervical and thoracic regions. Mean asymmetry indices (defined as the ratio between right and left sides) and standard deviations were then calculated for each level. Any sensory function measured in the PHN or NoPHN patient was defined as abnormal if the degree of asymmetry, that is, measured values between the affected and the unaffected skin areas, exceeded two standard deviations more than the mean of the control subjects.

Results

Clinical findings

Allodynia, tested by the brush method, was present in 33 of 38 tested (87%). Cases ranged from moderate to extreme allodynia. In the latter case (one third of tested cases) patients reported induced pain as completely unbearable (VAS 100 mm). The mean VAS before provocation was 26·5 (SD) 26·9 mm and after provocation 64·3 (SD) 29·5 mm. Although in most cases brushing caused some pain immediately, it steadily increased until the peak VAS was reached. The mean duration of time elapsed before maximum pain was 32·1 (SD) 24·8s. Hyperpathia was present in virtually all cases with allodynia; its mean duration was 41·5 (SD) 58·9s.

Brushing did not produce any painful sensations in the NoPHN cases during a one minute period.

There were 12 cases of ophthalmic PHN. In six of them, marked tenderness and allodynia was seen over the maxillary region but not the mandibular division. This tenderness did not follow an accurate anatomical distribution; rather it tended to be below the eye and on the cheek, but not usually on the ear or the upper lip. Also, in some patients this maxillary tenderness was so prominent that it resembled the trigger zones encountered in trigeminal neuralgia. In ten cases moving one to three eyebrow hairs caused a sensation of pain or tenderness while only a ticklish sensation was reported (by the patient) on the contralateral side. These patients had previously been diagnosed as having ophthalmic zoster only (according to the extent of the initial rash), with the exception of one patient in whom the case history suggested maxillary branch involvement.

In ten out of 12 patients, lateral skin stretch did not elicit any painful sensations. One patient reported slight pain and one marked pain.

Somatosensory thresholds

As mentioned previously, the thresholds were measured in at least two different places within the affected dermatome (and in the mirror-image area on the contralateral side of the body). Analysis of the data revealed that generally results were similar irrespective of the testing site. Therefore, in this report we concentrate only on the maximum pain area findings.

Results are shown in tables 3 and 4. Statistically significant differences between the affected area and the contralateral mirror area are present in all sensory tests measured in the PHN group. No such abnormalities were found in the NoPHN group.

The frequencies of abnormal tested sensory perception thresholds (defined as more than 2 SD above the mean of asymmetry indices derived from the control population, see Methods) are shown in table 5. In the NoPHN group, usually only solitary threshold abnormalities were encountered. Sensory deficits affecting two or more modalities occurred in 93% of PHN patients and in 10% of NoPHN patients. Two PHN patients (5%) and 12 NoPHN patients (60%) did not demonstrate any sensory abnormalities whatsoever.

Drug therapy did not seem to have any effect on the findings: 13/14 of unmedicated and 25/28 of medicated PHN patients showed sensory abnormalities of at least two different modalities. There were no temperature asymmetries.

Table 4 Threshold medians (and ranges) of the affected and unaffected skin areas in NoPHN patients (N = 20)

	Affected side	*Unaffected side*
Warm threshold (°C)	33·4 (31·8–44·6)	33·7 (31·8–41·2)
Cold threshold (°C)	28·8 (23·0–29·6)	28·8 (24·6–29·7)
Hot pain threshold (°C)	43·8 (31·9–46·7)	44·8 (38·9–47·1)
Tactile threshold ($\log_{10}$ 0·1 mg)	3·0 (2·4–4·1)	2·6 (1·7–3·6)
Pinprick threshold (g)	0·7 (0·2–3·8)	0·7 (0·2–2·8)
2-point discrimination (cm)	3·8 (1·5–10·0)	2·6 (1·5–10·0)
Vibration threshold (μm)	5·4 (2·8–52·0)	5·8 (1·8–23·0)

No significant differences between sides (for each comparison, $p < 0·10$, two-tailed; Wilcoxon matched-pairs test)

Discussion

These data corroborate the clinical impressions that patients with postherpetic neuralgia exhibit major sensory abnormalities. Sensory functions subserved by both large and small diameter populations seem to be affected although we cannot draw conclusions as to the actual ratio of the fibres preserved. In this respect similar results have been obtained from patients with painful diabetic polyneuropathy.[25]

It seems evident that people who recover from shingles without major pain or itch (all tested subjects in the NoPHN group had recovered in the first three months) are left with no or minor subclinical local neuropathy. This agrees with Noordenbos' view that as a rule sensory changes are lacking in patients who recover from shingles.[9] (Noordenbos did not state the number of patients he had observed). Similarly, Head and Campbell did not find any morphological changes in two of their cases (cases 20, 21) and correlate findings in the DRG, dorsal root and peripheral nerve to the severity of the eruption.[6] In turn, Higa *et al* found a relationship between antibody responses to varicella-zoster virus and the severity of skin lesions.[26] The obvious clinical conclusion one wishes to draw from the present data is that patients who complain about pain after shingles should have sensory changes if pain is to be related to postherpetic neuralgia; if none are found, other reasons for pain (such as musculoskeletal) should be looked for.

The dual nature of pain associated with PHN has been recognised.[12 14] For example, there is more or less constant pain present (described as burning, nagging, aching and stabbing by the patients)[12] and this obviously reflects spontaneous abnormal barrages somewhere along the somatosensory pathways. As both peripheral and central interruption of pain pathways independently abolish pain in PHN, although temporarily,[14 27 28] one must assume dysfunction at both levels, but the pathophysiological mechanisms involved remain elusive.

Alternatively, more may be speculated about allodynia, referred to by patients as "soreness" or "tenderness".[12] Our finding of 87% showing allodynia in response to toothbrush application closely resembles that of Watson *et al*.[29] By rubbing the skin with a cotton-tipped stick they found "hyperesthesia, dysesthesia or allodynia to light stroking" in 65% of their PHN patients. Our higher figures may simply reflect a more vigorous method of stimulation. The results are underlined by the additional finding of hair follicle movements producing pain in the tested patients. In healthy subjects, low frequency stimulation predominantly activates rapidly adapting low threshold mechanoreceptors and hair receptors.[30] In contrast, lateral skin stretch and maintained skin compression are associated with the activation of slowly adapting mechanoreceptors.[31] In this study, skin stretch failed to produce any pain in most patients that were tested. We also noticed the fairly common situation whereby patients spend much of their time pressing a hand over the painful region, or wearing an extra tight garment.[14]

These observations suggest that mechanical stimuli known to activate slowly adapting mechanoreceptors in healthy subjects do not provoke allodynia in postherpetic neuralgia whereas those stimuli which activate rapidly adapting mechanoreceptors do. Could allodynic pain be produced by non-nociceptive stimulation of other receptors than mechanoreceptors? Noordenbos has argued that all stimuli if applied long enough elicit pain in PHN.[9] In his study, multiple pinpricks caused, after a delay, an outbreak of pain spreading over large areas and slowly wearing off. Similarly, a hot test tube which did not cause any discomfort on normal skin produced, when applied to the zoster area, a steady increase over a minute or so in perceived sensation from faintly warm to hot and finally painful.[9] In their study Watson *et al* noted that pinching the skin resulted in hyperalgesia in 58% of their PHN patients.[29] It seems possible therefore that in PHN innocuous stimulation of A delta nociceptors may result in pain, similar to hyperalgesia after mechanical irritation.

In this study, however, we found no such broad-spectrum hyperalgesia. The patients did not usually find pinprick testing painful in spite of repeated needling. Cooling the affected skin slowly down to 5°C resulted in a pain response in 12 of 22 tested; but only four patients reported pain at a higher temperature than on the healthy side. Similarly, during heat induction only three of 40 patients felt pain at a lower temperature on the zoster area than on the contralateral side. In contrast, there were raised thresholds for warm or hot stimuli in 58% and 45% respectively, and lowered thresholds for cold in 50% of our cases. Lindblom and Verrillo describe in 11 patients with mainly post-traumatic neuralgias who showed two different responses to thermal stimuli: hypersensitive and hyposensitive.[32] Hypersensitivity was considered present if heat pain thresholds were low and cold pain thresholds raised compared with the intact skin. With this definition, our results show that in PHN the hyposensitive reaction to thermal stimuli is much more frequent than the hypersensitive reaction. Whereas hyperalgesia to thermal stimuli as a consequence of nerve trauma is reported to be common,[32 33] postherpetic neuralgia evidently represents an entity of its own with the characteristic feature of extreme hyperalgesia to mechanical stimuli but less so to thermal ones.

The question remains whether this mechanical allodynia is provoked by activation of intact RA I mechanoreceptors or whether it is the sign of other afferent receptors being sensitised to mechanical stimuli. Two facts in our study favour the mechanoreceptor theory: 1) even in cases where thermal thresholds were extremely pathological, being elevated to the tissue injury level, there was still mechanoreceptor sensitivity, 2) in a group of PHN patients, selective blocking of large diameter fibres abolished allodynia whereas that of small fibres did not (Nurmikko *et al*, submitted). Similar observations have been published in selective nerve injuries.[34]

One can also conjecture a role for the sympathetic system because of its postulated ability to sensitise mechanoreceptors in injured nerve endings.[35] Allodynia is a prominent feature of various sympathetically dependent pain conditions, notably reflex sympathetic dystrophy.[35] Is allodynia in PHN also, at least in part sympathetically maintained? Certainly, patients with PHN do report increase in pain in response to anxiety and exposure to cold. They

seem to experience bouts of cold and hot within the affected area, suggesting local autonomic instability. Also, sympathetic blocks have been reported to be of benefit even in PHN of more than one year[36] although not all authors agree.[2 3] Our results fail to show any sympathetic hyperfunction in patients with PHN, and, indeed, reflex sympathetic dystrophy is extremely rarely documented in postherpetic neuralgia.[37] This is not to say that the sympathetic system has no role in PHN. It is quite possible that its physiological fluctuations may modify pain or allodynia in PHN. Loh and Nathan noted that for a sympathetic block to be effective in chronic neuralgias, signs of sympathetic abnormality did not have to be present.[38] Recently, we have assessed the role of the sympathetic system by means of differential blocks and the results will be reported in a separate study (Nurmikko *et al* submitted).

Animal studies show that as a consequence of peripheral nerve injury there is a change of the receptive fields of the cut nerve in the dorsal horn. Those neurons which previously responded only to the territory of the cut nerve begin to respond to nearby intact nerves.[39 40] Whether this phenomenon, recently named somatotopic remodelling, happens in the sensory domain is not known.[41] From our findings we suggest that mechanical allodynia represents a state where second order neurons that primarily respond to noxious stimuli start responding to inputs travelling in the A beta fibres associated with RA I receptors. This central reorganisation also offers a plausible explanation for the discovery of extension of hyperesthesia outside the territory of the ophthalmic nerve in six of the twelve trigeminal PHN patients. In the acute stages of shingles, these patients, with one exception, were judged by primary care doctors and ophthalmologists to have ophthalmic involvement only. In epidemiological studies, maxillary involvement in acute states of shingles is rare[6 12] and it is unlikely that our patients had subclinical maxillary branch infection without eruption. In 1949 Russell *et al* observed that in ophthalmic zoster, blockade of the ipsilateral occipital nerve, as well as the contralateral ophthalmic or supratrochlear nerves, alleviated hyperesthesia,[42] an idea also suggesting that allodynia may actually extend outside the area innervated by the affected ophthalmic nerve. This cannot be explained by overlapping of dermatomes; there is very little overlap between the three divisions of the trigeminal nerve.[43] Somatotopic remodelling appears to be the most likely mechanism, although accurate repeated measurements from the beginning of the infection to the end stage of PHN would clarify this. Additional central contributions may arise from atrophic changes in the trigeminal nucleus which have been recently verified in pathological examinations.[44]

Our findings suggest that the physiopathological changes in PHN are likely to be in the CNS as well as in the PNS. This would place this narcotic-resistant non-nocigenic painful condition in the same category as other neurogenic pains of both central and peripheral origin, although its autonomic characteristics certainly differentiate it from some of them. Further investigation of acute herpes zoster is needed to discover if there are pathophysiological factors which will predict whether a given case is likely to recover without sensory deficit and without PHN, or to persist with sensory deficit and with the PHN which appears ineluctably to accompany it.

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